

What is claimed is:

## CLAIMS

- 5
1. A tip-electrode comprising:  
a housing defining a lumen for receiving an electrically conductive medium; and  
an electrically conducting surface for coupling to a voltage or current  
10 generator.
  2. The tip electrode of claim 1, wherein the housing comprises a target-facing end comprising an opening in communication with the lumen for delivering an agent through the opening to a target.
  - 15 3. The tip electrode of claim 1, wherein the lumen comprises an electrically conductive medium.
  4. The tip electrode of claim 1, wherein the housing comprises a tapered end.
  5. The tip electrode of claim 1, wherein the electrically conducting surface comprises a coating at least partially coating walls of the housing defining the  
20 lumen.
  6. The tip electrode of claim 1, wherein the tip-electrode comprises an element inserted into the lumen of the housing comprising the electrically conducting surface.
  7. The tip electrode of claim 6, wherein the element is a cylinder, rod, filament,  
25 or wire.
  8. The tip electrode of claim 6 or 7, wherein the electrically conducting surface is a structure penetrating the walls of the housing on one or both sides of the housing.

9. The tip electrode of claim 1, wherein the electrically conducting surface is a wire connected on the outside of the housing to a ring plate.
10. The tip electrode of claim 1, wherein the electrically conductive medium is a liquid.
- 5 11. The tip electrode of claim 1, wherein the electrically conductive medium is a gel.
12. The tip electrode of claim 1, wherein the electrically conductive medium comprises an agent for delivery to a target.
- 10 13. The tip electrode of claim 1, wherein the housing comprises a material selected from the group consisting of glass, fused silica, plastic, ceramic, an elastomeric material, a polymer, metal, a non-conducting material coated at least partially with a conducting material, and a conducting material coated at least partially with a non-conducting material.
- 15 14. The tip electrode of claim 2, wherein the housing further comprises a receiving end distal to the target-facing end and comprises an opening for receiving the electrically conductive medium.
15. The tip electrode of claim 1, wherein the tip-electrode further comprises a conducting surface which functions as a counter electrode.
- 20 16. The tip-electrode of claim 1, wherein the housing comprises a uniform inner diameter and uniform or varying outer diameter.
17. The tip-electrode of claim 1, wherein the housing comprises a uniform outer diameter and uniform or varying inner diameter.
18. The tip-electrode of claim 1, wherein the length of the tip electrode is less than about 10 cm.
- 25 19. The tip-electrode of claim 1, wherein the length of the tip electrode is less than about 500  $\mu\text{m}$ .

20. The tip-electrode of claim 1, wherein the length of the tip electrode is less than about 50  $\mu\text{m}$ .
21. The tip-electrode of claim 1, wherein the length of the tip electrode is less than about 1  $\mu\text{m}$ .
- 5 22. The tip-electrode of claim 2, wherein the diameter of the opening at the target-facing end is less than or equal to about 5000  $\mu\text{m}$ .
23. The tip-electrode of claim 2, wherein the diameter of the opening at the target-facing end is less than about 100  $\mu\text{m}$ .
24. The tip electrode of claim 2, wherein the diameter of the opening at the target-facing end is less than about 50 $\mu\text{m}$ .
- 10 25. The tip-electrode of claim 2, wherein the diameter of the opening at the target facing end is less than about 10 $\mu\text{m}$ .
26. The tip-electrode of claim 2, wherein the diameter of the opening at the target-facing end is less than about 1  $\mu\text{m}$ .
- 15 27. The tip-electrode of claim 2, wherein the diameter of the opening at the target-facing end is less than about 100 nm.
28. The tip-electrode of claim 2, wherein the diameter of the opening at the target-facing end is less than about 50 nm.
29. An electrode plate comprising at least one mounting point for receiving a tip electrode.
- 20 30. The electrode plate of claim 29, wherein the at least one mounting point comprises a flexible attachment point for receiving the tip electrode permitting vertical movement of a tip-electrode from the mounting point.
31. The electrode plate of claim 29, comprising a plurality of mounting points.
- 25 32. The electrode plate of claim 31, wherein the plate comprises a row of mounting points for forming a linear array of tip-electrodes.

33. The electrode plate of claim 31, wherein the plate comprises a plurality of rows of mounting points for forming a two-dimensional array of tip-electrodes.
34. The electrode plate of claim 31, wherein the center-to-center distance of each mounting point corresponds to the center-to-center distance of wells in an industry standard microtiter plate.
35. The electrode plate of claim 29, wherein the electrode plate comprises at least one interface point for a voltage or current generator.
36. The electrode plate of claim 29, wherein the electrode plate comprises at least one interface point for interfacing with a fluid delivery device.
37. The electrode plate of claim 29, wherein the electrode plate comprises at least two layers including a conducting layer and an insulating layer.
38. The electrode plate of claim 39 or 37, comprising a layer that functions as a counter electrode.
39. The electrode plate of claim 29, wherein the at least one mounting point comprises an aperture for receiving the tip-electrode.
40. The electrode plate of claim 29, wherein at least one tip-electrode is mounted to the electrode plate at the mounting point.
41. The electrode plate of any of claims 31-33, wherein a plurality of tip electrodes are mounted to the electrode plate.
42. The electrode plate of claim 29, wherein the plate comprises at least one microfluidic channel for delivering fluids to at least one tip electrode mounted to the plate.
43. A tip-electrode plate comprising a substantially planar plate on which at least one non-planar element is fabricated thereon, wherein an end of the non-planar element distal from the plate comprises an opening for exposing a target to an electric field and wherein inner walls of the non-planar element define a lumen.

44. The tip-electrode plate of claim 43, wherein the inner walls comprise an electrically conductive surface and/or the lumen comprises an electrically conductive medium.
- 5 45. The tip-electrode plate of claim 43, wherein the electrically conductive surface is a conductive coating which at least partially coats the inner walls of the reservoir.
46. The tip-electrode plate of claim 43, wherein the structure comprises a wire, rod or filament at the base of the lumen or penetrating one or both walls of the non-planar element.
- 10 47. The tip electrode plate of claim 43, wherein the end of the at least one non-planar element is tapered.
48. The tip electrode plate of claim 43, wherein the plate comprises a first layer comprising a plurality of reservoirs and a substantially planar second layer comprising a plurality of nonplanar elements elevated above the plate, wherein  
15 each nonplanar element comprises a target-facing opening centered above each reservoir in the first layer for exposing a target to an electric field, and wherein inner walls of the nonplanar element define a lumen communicating both with the reservoir and the opening.
49. The tip-electrode plate of claim 48, wherein the plate further comprises a  
20 counter electrode layer.
50. The tip electrode plate of claim 43 or 48, wherein reservoirs comprise an electrically conductive medium.
51. The tip electrode plate of claim 50, wherein the electrically conductive medium comprises an agent.
- 25 52. The tip electrode plate of claim 49, wherein the counter electrode layer contacts the electrically conductive medium.
53. The tip electrode plate of claim 43 or 48, wherein the reservoirs comprise an agent.

54. A kit comprising a tip electrode of claim 1 and a container for containing a target.
55. A kit comprising an electrode plate of claim 29 and at least one tip electrode for mounting on the electrode plate.
- 5 56. The kit of claim 55, further comprising a container for containing a target.
57. The kit of claim 55, wherein the electrode plate comprises at least one microfluidic channel.
58. The kit of claim 56, wherein the electrode plate and/or container comprises at least one microfluidic channel.
- 10 59. The kit of claim 56, wherein the container for containing the target is selected from the group consisting of a microtiter dish, a multi-well cell culture container, a petrie dish, polymeric substrate, a glass substrate, a microfluidic chip, and a membrane.
60. The kit of claim 55, wherein the kit further comprises at least one counter  
15 electrode.
61. The kit of claim 55, wherein the kit further comprises an electrically conductive medium for filling at least one tip-electrode.
62. The kit of claim 55, wherein the kit comprises at least one agent.
63. The kit of claim 55, wherein the kit comprises at least one cell.
- 20 64. A kit comprising a tip-electrode plate of claim 55, wherein the kit further comprises container for containing a target.
65. The kit of claim 64, wherein the tip-electrode plate and/or container further comprises at least one microfluidic channel.
- 25 66. The kit of claim 65, wherein the container for containing the target is selected from the group consisting of a microtiter dish, a multi-well cell culture container, a petrie dish, polymeric substrate, a glass substrate, a microfluidic chip, and a membrane.

67. The kit of claim 65, wherein the kit further comprises an electrically conductive medium for filling at least one reservoir.
68. The kit of claim 65, wherein the kit comprises at least one agent.
69. The kit of claim 65, wherein the kit comprises at least one cell.
- 5 70. A system comprising at least one tip electrode comprising:  
an electrically conducting surface in contact with an electrode plate  
and a housing defining a lumen for receiving an electrically conductive  
medium, wherein the housing comprises a target-facing end comprising an  
opening in communication with the lumen for delivering an agent through the  
10 opening to a target, wherein the electrode plate is connectable to a pulse  
generator for delivering a voltage or current pulse to the electrically  
conducting surface.
71. The system of claim 70, further comprising:  
15 a container for containing a target.
72. The system of claim 70, wherein the system further comprises a mechanism  
for positioning the at least one tip-electrode in proximity to a target.
73. The system of claim 70, wherein the system further comprises a pulse  
generator in communication with the electrode plate for delivering voltage or  
20 current pulses through the at least one tip electrode.
74. The system of claim 70, further comprising at least one counter electrode.
75. The system of claim 70, wherein the lumen of the at least one electrode tip  
comprises an electrically conductive medium.
76. The system of claim 75, wherein the electrically conductive medium  
25 comprises an agent.
77. The system of claim 75, wherein the system further comprises a delivery  
mechanism for delivering a fluid and/or an agent to at least one tip electrode.

78. The system of claim 77, wherein the delivery mechanism further comprises one or more of: a pumping mechanism, a mechanism for electroosmosis, or a mechanism for electrophoresis of an agent through the lumen of the tip electrode.
- 5 79. The system of claim 70, wherein the system comprises a plurality of tip electrodes, each in electrical contact with the electrode plate.
80. The system of claim 79, wherein electrical pulses transmitted through each tip electrode are independently controlled through a system processor.
81. The system of claim 79, wherein the plurality of tip electrodes are arrayed in a  
10 row.
82. The system of claim 79, wherein the plurality of tip electrodes arrayed in a plurality of rows.
83. The system of claim 71 or 79, wherein the electrode plate and/or container comprise one or more microfluidic channels.
- 15 84. The system of 70, wherein the system further comprises a detector, for detecting alteration of electrical properties or optical properties of a target proximity to a tip electrode and/or delivery of a fluid and/or agent to the target.
85. The system of claim 70, wherein the at least one tip electrode is detachable  
20 from the electrode plate.
86. The system of claim 70, wherein the at least one tip-electrode is an integral part of the electrode plate.
87. The system of claim 86, wherein the electrode plate comprises a first layer comprising a plurality of reservoirs and a substantially planar second layer  
25 comprising a plurality of nonplanar elements elevated above the plate forming the tip electrodes, wherein the target-facing opening of the tip electrode is centered above each reservoir in the first layer, and wherein the lumen of the tip electrode communicates with the reservoir.



88. The system of claim 70, wherein the lumen of the at least one tip electrode comprises an electrically conductive medium.
89. The system of claim 70, wherein the housing of the at least one tip electrode comprises a tapered end.
- 5 90. The system of claim 70, wherein the electrically conducting surface of the at least one tip electrode comprises a coating at least partially coating walls of the housing defining the lumen.
91. The system of claim 70, wherein the electrically conducting surface comprises an element comprising an electrically conducting surface inserted into the  
10 lumen of the housing.
92. The system of claim 70, wherein the element is a cylinder, rod or wire.
93. The system of claim 70, wherein the electrically conducting surface is a structure penetrating the walls of the housing on one or both sides of the housing.
- 15 94. The system of claim 70, wherein the electrically conducting surface is a wire connected on the outside of the housing to a ring plate.
95. The system of claim 70, wherein the electrically conductive medium is a liquid.
96. The system of claim 70, wherein the electrically conductive medium is a gel.
- 20 97. The system of claim 70, wherein the electrically conductive medium comprises an agent for delivery to a target.
98. The system of claim 70, wherein the housing comprises a material selected from the group consisting of glass, fused silica, plastic, ceramic, an elastomeric material, a polymer, metal, a non-conducting material coated at  
25 least partially with a conducting material, and a conducting material coated at least partially with a non-conducting material.

99. The system of claim 70, wherein the housing of the at least one tip-electrode further comprises a receiving end distal to the target-facing end and comprises an opening for receiving the electrically conductive medium.
100. The system of claim 70, wherein the at least one tip-electrode and/or electrode plate further comprises a conducting surface that functions as a counter electrode.
101. The system of claim 70, wherein the housing of the at least one tip electrode comprises a uniform inner diameter and uniform or varying outer diameter.
102. The system of claim 70, wherein the housing of the at least one tip electrode comprises a uniform outer diameter and uniform or varying inner diameter.
103. The system of claim 70, wherein the length of the at least one tip electrode is less than about 10 cm.
104. The system of claim 70, wherein the length of the at least one tip electrode is less than about 500  $\mu\text{m}$ .
105. The system of claim 70, wherein the length of the at least one tip electrode is less than about 50  $\mu\text{m}$ .
106. The system of claim 70, wherein the length of the at least one tip electrode is less than about 1  $\mu\text{m}$ .
107. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than or equal to about 5000  $\mu\text{m}$ .
108. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than about 100  $\mu\text{m}$ .
109. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than about 50  $\mu\text{m}$ .
110. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than about 10  $\mu\text{m}$ .

111. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than about 1  $\mu\text{m}$ .
112. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than about 100 nm.
- 5 113. The system of claim 70, wherein the diameter of the opening at the target-facing end of the at least one tip electrode is less than about 50 nm.
114. The system of claim 70, the electrode plate comprises at least one mounting point for receiving a tip electrode, and wherein the at least one mounting point comprises a flexible attachment point for receiving the tip electrode permitting  
10 vertical movement of a tip-electrode from the mounting point.
115. The system of claim 114, wherein the electrode plate comprises a plurality of mounting points.
116. The system of claim 114, wherein the plate comprises a row of mounting points for forming a linear array of tip-electrodes.
- 15 117. The system of claim 114, wherein the plate comprises a plurality of rows of mounting points for forming a two-dimensional array of tip-electrodes.
118. The system of claim 114, wherein the center-to-center distance of each mounting point corresponds to the center-to-center distance of wells in an industry standard microtiter plate.
- 20 119. The system of claim 114, wherein the electrode plate comprises at least one interface point for a voltage or current generator.
120. The system of claim 114, wherein the electrode plate comprises at least one interface point for interfacing with a fluid delivery device.
121. The system of claim 114, wherein the electrode plate comprises at least two  
25 layers including a conducting layer and an insulating layer.
122. The system of claim 114 or 121, wherein the electrode plate comprises a layer which functions as a counter electrode.

123. The system of claim 114, wherein the at least one mounting point comprises an aperture for receiving the tip-electrode.
124. The system of claim 71, wherein the electrode plate and/or container comprises at least one microfluidic channel.
- 5 125. The system of claim 70, further comprising a processor for controlling one or more parameters selected from the group consisting of: delivery of fluid to the at least one tip electrode, delivery of at least one agent to at least one tip electrode, filling of the tip electrode with an electrically conductive medium, voltage or current pulse parameters, scanning of the electrode plate comprising  
10 the at least one tip electrode relative to a target, scanning of a target relative to a tip electrode, vertical movement of a tip electrode, electrophoresis through a tip electrode, electroosmosis through a tip electrode, pumping of fluid through a tip electrode, and function of a system detector.
126. The system of claim 125, wherein the voltage or current pulse parameters are  
15 selected from the group consisting of pulse duration, waveform, and pulse amplitude.
127. The system of claim 125 or 126, wherein the system further comprises a user device comprising a graphical interface for displaying operations of the system and/or for altering system parameters.
- 20 128. The system according to claim 84, wherein the system further comprises a read-out device for displaying output from the detector.
129. The tip electrode of claim 1, wherein the tip electrode comprises a flexible portion.
130. The system of claim 70, wherein the at least one tip electrode comprises a  
25 flexible portion.
131. The system of claim 70, wherein the system further comprises a positioning mechanism for restricting vertical movement of the at least one tip electrode.

132. The system of claim 131, wherein the positioning mechanism is mounted to the target-facing end of the at least one tip electrode.
133. The system of claim 131, wherein the positioning mechanism is an integral part of the tip electrode.
- 5 134. The tip electrode of claim 2, wherein the tip comprises holes in the portion of the tip proximal to the target facing end.
135. The electrode plate of claim 41, wherein at least one tip comprises holes in a portion of the tip proximal to its target facing end.
136. A method, comprising
- 10 exposing a sample comprising a target and at least one non-target component to a focused electric field, wherein the focused electric field selectively alters the properties of the target.
137. The method of claim 136, wherein the target comprises a biological membrane.
- 15 138. The method of claim 137, wherein the target is selected from the group consisting of: a population of cells, a single cell, an intracellular organelle, a vesicle, a liposome, a molecule, a group of molecules, a nucleic acid, protein, polypeptide, peptide; enzyme; carbon fiber; chemical reactant and a surface.
139. The method of claim 136, wherein the target is suspended in a liquid
- 20 comprising at least one non-target.
140. The method of claim 136, wherein the target is associated with a substrate.
141. The method of claim 140, wherein the substrate comprises an array.
142. The method of claim 140, wherein the substrate comprises a microtiter dish.
143. The method of claim 136, wherein the electric field is provided by a tip
- 25 electrode of claim 1.

144. The method of claim 136, wherein the method comprises exposing each of a plurality of targets in a sample comprising a plurality of non-target components to a focused electric field.
145. The method of claim 144, wherein each focused electric field is independently tunable.
146. The method of claim 144, wherein a plurality of tip electrodes of claim 1 provide the focused electric fields.
147. The method of claim 146, wherein the plurality of targets are exposed sequentially or in parallel to the plurality of focused electric fields.
148. The method of claim 146, wherein the plurality of tip electrodes are arrayed on an electrode plate.
149. The method of claim 148, wherein each of the plurality of tip electrodes is positioned over the well of a microtiter plate.
150. The method of claim 148, wherein each of the plurality of tip electrodes is positioned over a spot on a substrate on which a target is located.
151. The method of claim 136, wherein the target comprises a biological membrane and wherein the exposing generates pores in the membrane.
152. The method of claim 136 or 151, wherein the method further comprises exposing the target to an agent.
153. The method of claim 137, wherein the method further comprises exposing the target to an agent, and introducing the agent into a compartment defined by the membrane.
154. The method of claim 152, wherein exposure to the electric field and exposure to the agent is coordinated.
155. The method of claim 136, wherein the target comprises a single cell in a confluent cell culture.

156. The method of claim 136, wherein the target comprises less than the total number of cells in a confluent cell culture.
157. The method of claim 136, wherein the target comprises less than about 500 cells in a confluent cell culture.
- 5 158. The method of claim 136, wherein the method further comprises altering conditions of a solution in which the target is bathed.
159. The method of claim 151, wherein the electric field is generated by a tip electrode of claim 1, and wherein the target is further exposed to an agent delivered by the tip electrode.
- 10 160. The method of claim 143 or 151, wherein the tip electrode is coupled to a plate comprising at least one channel in fluid communication with the lumen of the tip electrode.
161. The method of claim 140, wherein the substrate comprises at least one channel in fluid communication with the target.
- 15 162. The method of claim 161, wherein the target is exposed to an agent in the fluid in the at least one channel.
163. The method of claim 161, wherein the substrate comprises a plurality of channels in fluid communication with the target.
164. The method of claim 161, wherein a plurality of agents and/or buffer is delivered sequentially or in parallel to the target from the plurality of channels.
- 20 165. The method of claim 161, wherein the target is exposed to at least one fluid stream from the at least one channel.
166. The method of claim 161, wherein the target is scanned across the at least one fluid stream by moving the target, moving the substrate, moving both the substrate and the target and/or by varying pressure at the at least one channel of the substrate.
- 25 167. The method of claim 136, further comprising detecting the altered property.

168. The method of claim 136, further comprising monitoring one or more parameters of the electric field.
169. The method of claim 168, further comprising monitoring one or more parameters of the electric field.
- 5 170. The method of claim 168, further comprising altering a parameter of the electric field in response to detection of the altered property.
171. The method according to claim 161, wherein the target is exposed to the fluid stream by delivering a fluid stream from a channel outlet in proximity to the target.
- 10 172. The method according to claim 171, where the fluid comprises an agent.
173. The method according to claim 172, wherein delivery of the fluid stream is coordinated with exposure of the target to the electric field.
174. The method of claim 152, wherein the agent is selected from the group consisting of genes; gene analogs; RNA; RNA analogs; siRNA; antisense  
15 oligonucleotides; ribozymes; DNA; DNA analogs; aptamers; colloidal particles; nanoparticles; receptors; receptor ligands; receptor antagonists; receptor agonists; receptor blockers; enzymes; enzyme substrates; enzyme inhibitors; enzyme modulators, proteins; protein analogs; polypeptides; polypeptide analogs; amino acids; amino acid analogs; peptides; peptide  
20 analogs; metabolites; metabolite analogs; oligonucleotides; oligonucleotide analogs; antigens; antigen analogs; haptens; hapten analogs; antibodies; antibody analogs; organelles; organelle analogs; cell nuclei; cell fractions; bacteria; viruses; viral particles; gametes; inorganic ions; organic ions; metal; agents that affects cellular chemistry; agents that affect the cytoskeleton,  
25 agents that affect polymers and combinations thereof.
175. The method of claim 159 and 172, wherein the agent is selected from the group consisting of genes; gene analogs; RNA; RNA analogs; siRNA; antisense oligonucleotides; ribozymes; DNA; DNA analogs; aptamers; colloidal particles; nanoparticles; receptors; receptor ligands; receptor



- antagonists; receptor agonists; receptor blockers; enzymes; enzyme substrates; enzyme inhibitors; enzyme modulators, proteins; protein analogs; polypeptides; polypeptide analogs; amino acids; amino acid analogs; peptides; peptide analogs; metabolites; metabolite analogs; oligonucleotides; oligonucleotide analogs; antigens; antigen analogs; haptens; hapten analogs; antibodies; antibody analogs; organelles; organelle analogs; cell nuclei; cell fractions; bacteria; viruses; viral particles; gametes; inorganic ions; organic ions; metal; agents that affects cellular chemistry; agents that affect the cytoskeleton, agents that affect polymers and combinations thereof.
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- 10 176. The method of claims 152, wherein the agent alters a condition of a solution in which the target is bathed.
177. The method of claims 159 and 172, wherein the agent alters a condition of a solution in which the target is bathed.
178. The method of claim 172, wherein the condition is pH, temperature, ionic strength, osmolarity, viscosity and combinations thereof.
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179. The method of claim 177, wherein the condition is pH, temperature, ionic strength, osmolarity, viscosity and combinations thereof.
180. The method of claim 136, wherein the electric field induces a dipole in one or more target molecules.
- 20 181. The method of claim 136, wherein the electric field causes one or more target molecules to stretch, move, bind, react, and/or denature.
182. The method of claim 136, wherein the target is a surface and the tip delivers molecules for patterning the surface in the presence of the electric field with a plurality of molecules, macromolecules, cells, or combinations thereof.
- 25 183. The method of claim 151, wherein the biological membrane is exposed to the agent before, during, and/or after exposure to the electric field.
184. The method of claim 151, wherein the agent is a label.

185. The method of claim 151, wherein the label interacts with an intercellular molecule or intraorganellar molecule to produce a detectable signal or reactant, and wherein the method further comprises the step of detecting the detectable signal or reactant.
- 5 186. The method of claim 151, further comprising the step of separating and/or concentrating molecules, ions, and/or polymers in lumen of the tip.
187. The method of claim 186, wherein the polymers are selected from the group consisting of nucleic acids, proteins, polypeptides, peptides, carbohydrates, and combinations thereof.
- 10 188. The method of claim 151, wherein the target is pre-loaded with half of a FRET pair and the method further comprises the step of exposing the target to the other half of the FRET pair during and/or after exposure to the electric field, and wherein the production of a signal indicates confirms pore formation.
- 15 189. The method of claim 151, further comprising transferring solutes from the medium outside a compartment defined by the membrane into the compartment defined by the membrane.
190. The method of claim 151, further comprising transferring solutes from the medium inside the compartment defined by the membrane into a solution outside the membrane.
- 20 191. The method of claim 189 or 190, wherein the biological membrane is a cell membrane.
192. The method of claim 189 or 190, wherein the biological membrane is an the membrane of an intracellular organelle.
- 25 193. The method of claims 152, wherein the agent reacts with an intracellular molecule, macromolecule, polymer ion, protein, polypeptide, peptide, or nucleic acid, to produce a detectable product, and wherein the method further comprises detecting the detectable product.
194. The method of claims 159 and 172, wherein the agent reacts with an

intracellular molecule, macromolecule, polymer ion, protein, polypeptide, peptide, or nucleic acid, to produce a detectable product, and wherein the method further comprises detecting the detectable product.

- 5 195. The method of claim 189, further comprising detecting a response of the compartment to internalization of the agent.
- 10 196. The method of claim 189 wherein detection is performed by monitoring capacitance, voltametry, amperometry, CARS (coherent anti-stokes raman scattering), SERS (surface-enhanced raman scattering), phosphorescence, chemoluminescence, UV-VIS-IR absorption, quartz crystal microbalance, and surface plasmon resonance.
197. The method of claim 144, wherein the plurality of targets are localized at discrete locations on a substrate or in solution and separated from other targets by a physical barrier.
- 15 197. The method of claim 136, wherein the target is a cell of a selected type and the non-target is a cell of a different type.
198. The method of claim 136, wherein the target is an organelle of a selected type and the non-target is a cell of a different type.
- 20 199. A method of screening for an agent which alters an interaction between a first intracellular component and a second intracellular component, comprising:  
contacting a cell comprising the first intracellular component and the second intracellular component with the agent;  
exposing the cell to a focused electric field using a tip electrode of claim 1 under conditions for generating pores in the cell, and  
detecting a change in the interaction.
- 25 200. The method of claim 199, wherein the exposing step occurs before, during, and/or after the contacting step.
201. The method of claim 199, wherein the first and/or second component is labeled and the method comprises detecting a change in a signal produced by the label after the exposing.

202. The method of claim 199, wherein the method comprises detecting the presence or absence of, or a change in, a reaction that occurs when the first and second component interact.
203. The method of claim 199, wherein the method comprise detecting the presence or absence of, or a change in a cellular or extracellular function or phenotype associated with the interaction of the first and second component.
204. The method of claim 199, wherein the interaction comprises binding of the first and second component.
205. The method of claim 199 wherein the first and second component are independently selected from the group consisting of an intracellular molecule, macromolecule, metabolite, polymer, protein, polypeptide, peptide, nucleic acid, nucleobase, nucleotide, vesicle, cell membrane component, organelle and combinations thereof.
206. The method of claim 205, wherein the protein comprises a receptor, ligand, enzyme, cytoskeletal protein, signaling protein, ion channel, organelle membrane protein, or cell membrane protein.
207. The method of claim 199, wherein the agent is selected from the group consisting of genes; gene analogs; RNA; RNA analogs; siRNA; antisense oligonucleotides; ribozymes; DNA; DNA analogs; aptamers; colloidal particles; nanoparticles; receptors; receptor ligands; receptor antagonists; receptor agonists; receptor blockers; enzymes; enzyme substrates; enzyme inhibitors; enzyme modulators, proteins; protein analogs; polypeptides; polypeptide analogs; amino acids; amino acid analogs; peptides; peptide analogs; metabolites; metabolite analogs, oligonucleotides; oligonucleotide analogs; antigens; antigen analogs; haptens; hapten analogs; antibodies; antibody analogs; organelles; organelle analogs; cell nuclei; cell fractions; bacteria; viruses; viral particles; gametes; inorganic ions; organic ions; metal; agents that affects cellular chemistry; agents that affect the cytoskeleton, agents that affect polymers and combinations thereof.

208. The method of any of claims 199-207, wherein the agent is an agonist, antagonist or inhibitor of the first or second component.
209. The method of any of claims 199-207, wherein the agent modulates a signaling pathway.
- 5 210. The method of any of claims 199-207, wherein the agent modulates a metabolic pathway.
211. The method of any of claims 199-207, wherein the first component is an intracellular receptor and the second component is a ligand which binds the intracellular receptor.
- 10 212. The method of claim 199, wherein the first and/or the second component is introduced into the cell before, during, and/or after the exposing step.
213. A method of screening for an agent which binds to an intracellular component comprising:
- 15           contacting a cell comprising the intracellular component with a candidate binding agent;
- exposing the cell to a focused electric field using a tip electrode of claim 1 under conditions for generating pores in the cell, and
- detecting binding of the agent to the component.
- 20 214. The method of claim 213, wherein the agent and/or intracellular component is labeled and the method comprises detecting formation of a complex between the agent and the intracellular component.
215. The method of claim 213, wherein the method further comprises detecting a phenotype associated with binding.
216. The method of claim 213, wherein the method further comprises detecting a reaction produced when the intracellular component binds to an agent.
- 25 217. The method of claim 216, wherein the reaction comprises an increase in levels of a signaling molecule.

218. The method of claim 217, wherein the signaling molecule is selected from the group consisting of  $\text{Ca}^{2+}$ , cAMP, and  $\text{K}^{+}$ .
219. The method of claim 213, wherein the intracellular component comprises an intracellular receptor, the cytoplasmic domain of a cell membrane molecule, or an enzyme.
220. The method of claim 213, wherein the agent is selected from the group consisting of genes; gene analogs; RNA; RNA analogs; siRNA; antisense oligonucleotides; ribozymes; DNA; DNA analogs; aptamers; colloidal particles; nanoparticles; receptors; receptor ligands; receptor antagonists; receptor agonists; receptor blockers; enzymes; enzyme substrates; enzyme inhibitors; enzyme modulators, proteins; protein analogs; polypeptides; polypeptide analogs; amino acids; amino acid analogs; peptides; peptide analogs; metabolites; metabolite analogs, oligonucleotides; oligonucleotide analogs; antigens; antigen analogs; haptens; hapten analogs; antibodies; antibody analogs; organelles; organelle analogs; cell nuclei; cell fractions; bacteria; viruses; viral particles; gametes; inorganic ions; organic ions; metal; agents that affects cellular chemistry; agents that affect the cytoskeleton, agents that affect polymers and combinations thereof.
221. The method of claim 213, wherein the agent is delivered to the cell using electrophoresis or electroosmosis.